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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN THE MATTER OF:

U.S. Patent Application Serial no. 10/815,509

Inventors: Bolton, Anthony R. et al

Filed: March 31, 2004;

Title: "Treatment of Endothelin-Related Disorders";

Group Art Unit: 1616;

Examiner: Arnold, Ernst V.;

Attorney docket: 355908-3951

DECLARATION

I, Dr. ELDON RAYMOND SMITH, OC, MD., FRCP(C), FAHA, cardiologist, of #16, 1901

Varsity Estates NW, Calgary, Alberta, Canada T3B 4T7, hereby declare:

1. THAT I am currently Professor Emeritus, Faculty of Medicine at the University of Calgary. Previously, I was a Professor in the Faculty of Medicine at the University of Calgary, a position I have held since 1980. During that period, I have at times been Head of the Division of Cardiology, Head of the Department of Medicine, Associate Dean, Clinical Affairs, and Dean of the Faculty of Medicine at the University of Calgary. Also during the period from 1980 to date, I have successively held the positions of Chief of the Cardiology Division, Director of the Department of Medicine, and Physician, at Foothills Hospital, Calgary. During my career, I have received a number of distinctions and awards for my work in cardiovascular medicine. I am cited in "Who's Who in America," in "American Men and Women of Science," and in "Who's Who in Medicine and Health Care." Recently, I was appointed an Officer of the Order of Canada, the highest civilian

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honour granted by the Canadian government. The Order of Canada recognizes a lifetime of achievement and merit of a high degree, especially in service to Canada or to humanity at large. I am a member of the Council of the Canadian Cardiovascular Society, having served as its President from 1992 - 1994. I am the Editor-in-Chief, Canadian Journal of Cardiology. I am author or co-author of over 250 research articles published in various learned journals, in the field of cardiology. Accordingly, I believe that I am well qualified to express expert opinion on technical matters in the field of cardiology.

2. THAT I am, on a part-time basis, Vice-President of Scientific Affairs of Vasogen Inc., the parent company of the owner of the patent application identified above, and I have been a member of the Scientific Advisory Board of the said Vasogen Inc.
3. THAT I have read the disclosure and claims of the patent application, the prior art cited by the Examiner in the Examiner's action mailed March 20, 2006, and the Examiner's action dated March 20, 2006, in respect of the patent application.
4. Primary pulmonary hypertension (PPH) is a disease of the pulmonary arteries of unknown etiology, affecting mostly younger people and more often women. PPH is characterized by progressive shortness of breath and fatigue and most affected patients die within 4 years of diagnosis.
5. Pulmonary hypertension can also be secondary, particularly developing because of left heart disease leading to congestive heart failure. This occurs because of the inability of

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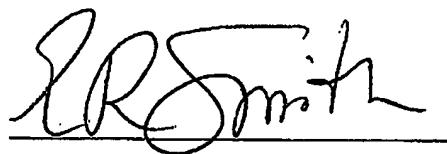
the left ventricle to empty appropriately (systolic heart failure) or to fill adequately (diastolic heart failure) and because of the resultant elevation in the diastolic pressure in the left ventricle which is passively transmitted to the left atrium and subsequently to the pulmonary veins and arteries. This secondary form of pulmonary hypertension is therefore very common, usually not as severe as primary pulmonary hypertension and responds to treatment of the left heart failure.

6. Primary pulmonary hypertension occurs in the absence of disease of the left ventricle or the presence of congestive heart failure (although patients with primary pulmonary hypertension do develop congestive heart failure secondary to failure of the RIGHT ventricle). Moreover, there are characteristic pathologic changes in the pulmonary arterial wall in PPH which are not observed when pulmonary hypertension develops secondary to left ventricular disease leading to congestive heart failure. As such, PPH and pulmonary hypertension which develops secondary to congestive heart failure are different conditions with different etiologies. Moreover, many of the treatments that have proven effective in secondary pulmonary hypertension are not effective in (and occasionally may worsen) primary pulmonary hypertension.
7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the

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validity of the application or any patent issued thereon.

EXECUTED at Calgary, Alberta, Canada, this 25th day of July, 2006.

A handwritten signature in black ink, appearing to read "E.R. Smith". The signature is fluid and cursive, with a horizontal line drawn underneath it.

Eldon R. Smith